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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,558	BECKER ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *422-429,431-440,464 and 466-479* is/are pending in the application.

4a) Of the above claim(s) *466-472* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *422-429,431-440 and 464* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

DETAILED ACTION

Response to Amendment

Newly submitted claims 473-479 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

New claims 473-479, added with the amendment filed 1/19/2005, are drawn to a method of determining the presence of a nucleic acid analyte in a sample and therefore, properly grouped with the method of Group II (clams 441-463), which was not elected, see reply filed 1/22/2003. Therefore, new claims 473-479 are withdrawn.

Further, since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 473-479 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of the Application

Claims 422-440 and 466-479 are currently pending in the instant application. Claims 473-479 are withdrawn. Claims 430 and 434-439 are cancelled. Claims 422-429, 431-433, 440, 464 and 466-472 are currently under examination.

Information Disclosure Statement

Applicants requests Examiner consider references contained in the information disclosure statement filed on 09/19/2005. The references contained in the information disclosure statement filed on 01/19/2005 have been considered, however an information disclosure statement fee should be charged for the reasons specified in 37 CFR 1.97(e).

Response to Arguments

The rejection of record of claims 422, 426, 429 and 440 under 35 U.S.C. 102(b) as being anticipated by Lubini et al. (Current Biology Vol. 1, No. 1, 1994, pp. 39-45) is withdrawn in response to Applicant's arguments filed 1/19/2005.

Applicant's arguments filed 01/19/2005 on the rejection of record of claims 422-440 and 464 under 35 U.S.C. 102(e) or 102(a) as being anticipated by Kool et al. (US Patent No. 5,514,546) have been fully considered but they are not persuasive. Applicant argues that Kool et al. discloses a stem-loop oligonucleotide having a loop domain comprised of a parallel binding (P) domain and an anti-parallel binding (AP) domain wherein both strands bind to a nucleic acid target. Applicants point out that the claimed hybridization probe forms a double-stranded hybrid with the nucleic acid analyte. Applicant further argues that the use of 2'-O-methyl ribose in Kool et al. is used in the P and AP domains as opposed to the double-stranded stem domain.

These arguments have been considered but are not persuasive because the oligonucleotide taught by Kool et al. can form a double-stranded hybrid with the nucleic acid

target see column 10, lines 1-5 which states "...a target:stem-loop oligonucleotide complex can be partially two stranded and partially three-stranded..." and see Figure 1. Further, the oligonucleotides taught by Kool et al. can contain a 2'-O-methyl in any domain of the stem-loop oligonucleotide (see column 13 and column 19, lines 10-50 and 20-30, respectively), which encompasses the first base region of the claimed probe.

Therefore, the rejection of record of claims 422-440 and 464 under 35 U.S.C. 102(e) or 102(a) as being anticipated by Kool et al. (US Patent No. 5,514,546) is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 422-428, 432-433, 440 and 466-472 rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550).

Claim 422 of the instant application is drawn to a hybridization assay probe comprising a detectable label and first and second base regions capable of hybridizing to each other to form a hybrid wherein at least one ribonucleotide is modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety and further wherein the probe forms a stable double-stranded hybrid with the nucleic acid analyte. Claim 22 is further limited wherein the portion of the first base region capable of forming a hybrid with the second base region includes a cluster of at least 4

ribonucleotides modified to include a 2'-O-alkyl substitution or contains one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution. The claims recite the probe includes a conjugate molecule joined at a site within the cluster of the first base region and the nucleic acid analyte comprises RNA or ribosomal RNA. The claims further recite the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

Agrawal et al. teach an oligonucleotide comprising self-complementary regions wherein the first and second base regions are capable of hybridizing to each other to form a hybrid (see page 15, lines 1-30). Agrawal et al. further teach the oligonucleotide can form a stable double-stranded hybrid with the nucleic acid target (see page 8, lines 23-35 and Figure 6) and the target nucleic acid sequence can be any nucleic acid sequence, which encompasses RNA and ribosomal RNA (see page 10, lines 14-36). Agrawal et al. further teach the self-complementary regions can contain one or more modified ribonucleotides, which encompasses a cluster of 4, wherein the ribonucleotide is a 2'-O-methyl substitution and further teach the self-complementary regions can contain DNA (see page 16, lines 24-36). Agrawal et al. further teach the incorporation of a conjugate molecule in the self-complementary regions, which includes the first base regions (see page 17, lines 1-12).

Since the structure of the claimed probe was taught by Agrawal et al., the claimed functions "for use in determining the presence of nucleic acid analyte in a sample" would have been an inherent property of the oligonucleotide taught by Agrawal. Note MPEP 2112.01 states in part "...[w]here the claimed and prior art products are identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established."

Therefore, Agrawal et al. anticipates claims 422-428, 432-433, 440 and 466-472 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 422, 424, 425-426, 429, 431-433, 440 and 469-472 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubini et al. (Current Biology 1994, Vol.1, No.1, pages 39-45) in view of Tyagi et al. (U.S. Patent Number 5,925,517).

Claim 422 of the instant application is drawn to a hybridization assay probe comprising a detectable label and first and second base regions capable of hybridizing to each other to form a hybrid wherein at least one ribonucleotide is modified to include a 2'-O-alkyl substitution, namely a 2'-O-methyl, to the ribofuranosyl moiety and further wherein the probe forms a stable double-stranded hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid. Claim 22 is further limited wherein the portion of the first base region capable of forming a hybrid with the second base region includes a cluster of at least 4 ribonucleotides modified to include a 2'-O-alkyl substitution or contains one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution. The claims recite the probe includes a conjugate

molecule joined at a site within the cluster of the first base region, the first and second base regions are contained within an oligonucleotide that is between 10 to 100 bases in length and wherein the detectable label comprises a fluorescent molecule and further wherein the nucleic acid analyte comprises RNA or ribosomal RNA.

Lubini et al. teach the sequence of a self-complementary 2'-O-methylated RNA-DNA chimera wherein only the RNAs (having a ribofuranosyl moiety) are the nucleic acids that are methylated (see Figure 1, page 40). Lubini et al. further teach the 2'-O-methyl modification is more stable that the unmodified sequence (see abstract) and further teach the sequence of the self-complementary oligonucleotides contains some 2'-O-methylated nucleotides (in italics) and the DNA residues are not methylated (in bold). Additionally, Lubini et al. teach oligonucleotides in the range between 10 to 100 bases in length (see Figure 1, page 40).

Since the structure of the claimed probe was taught by Lubini et al., the claimed functions "for use in determining the presence of nucleic acid analyte in a sample" would have been an inherent property of the oligonucleotide taught by Lubini et al. Note MPEP 2112.01 states in part "...[w]here the claimed and prior art products are identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established."

Lubini et al. does not teach an oligonucleotide probe comprising a detectable label, namely a fluorescent molecule.

Tyagi et al. teach oligonucleotides comprising self-complementary regions and further comprise a detectable label, namely a fluorescent label (see column 15 and 16, lines 40-43 and 23-27, respectively).

It would have been obvious for one of skill in the art to incorporate a detectable label, as taught by Tyagi et al. into an oligonucleotide, as taught by Lubini et al.

One would have been motivated to incorporate a detectable label, as taught by Tygai et al. into an oligonucleotide because oligonucleotides containing detectable labels are useful to detect a probe that is hybridized to a target nucleic acid and further useful in the production of nucleic acids in synthesis reactions.

Finally, one would have had an expectation of success given that Tyagi et al. specifically teach detection of a probe that is hybridized to a target nucleic acid (see Example VIII).

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 422-429, 431-433, 440, 464 and 466-472 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (U.S. Patent Number 5,514,551) in view of Agrawal et al. (WO 94/01550).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the

application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claim 422 of the instant application is drawn to a hybridization assay probe comprising a detectable label and first and second base regions capable of hybridizing to each other to form a hybrid wherein at least one ribonucleotide is modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety and further wherein the probe forms a stable double-stranded hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid. Claim 22 is further limited wherein the portion of the first base region capable of forming a hybrid with the second base region includes a cluster of at least 4 ribonucleotides modified to include a 2'-O-alkyl substitution or contains one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution. The claims recite the probe includes a conjugate molecule joined at a site within the cluster of the first base region, the first and second base regions are contained within an oligonucleotide that is between 10 to 100 bases in length and wherein the detectable label comprises a fluorescent molecule and further wherein the nucleic acid analyte comprises RNA or ribosomal RNA. The claims further recite the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution and the target sequence contained with the nucleic acid analyte includes a double-stranded region.

Yang et al. teach a hybridization assay probe comprising first and second base regions capable of hybridizing to each other to form a hybrid (see column 8, lines 36-50). Yang et al. further teach the hybridization assay probes can contain a detectable label, namely a fluorescent label (see column 17, lines 31-36). Yang et al. teach the oligonucleotide is between 10 to 100 nucleotides in length and the target nucleic acid can be any single or double-stranded nucleic acid, which includes RNA or ribosomal RNA (see column 6, lines 56-68). Yang et al. further teach the probe forms a stable double-stranded hybrid with the nucleic acid analyte target and not with a non-targeted nucleic acid (see column 7, lines 44-52). Yang et al. does not teach the substitution of the ribofuranosyl moiety is a 2'-O-methyl substitution and further does not teach the probe contains a conjugate molecule wherein the conjugate molecule is joined at a site located with the cluster of the first base region.

Agrawal et al. teach the self-complementary regions can contain one or more modified ribonucleotides, which encompasses a cluster of 4, wherein the ribonucleotide is a 2'-O-methyl substitution and further teach the self-complementary regions can contain DNA (see page 16, lines 24-36). Agrawal et al. further teach the incorporation of a conjugate molecule in the self-complementary region, which includes the first base regions (see page 17, lines 1-12).

It would have been obvious for one of skill in the art to substitute the 2'-O-methyl, as taught by Agrawal et al. with the riobfuranosyl moiety in the self complementary region of the probe taught by Yang et al.

One would have been motivated to substitute the 2'-O-methyl, as taught by Agrawal et al. with the riobfuranosyl moiety in the self complementary region because modifying the ribofuranosyl moiety increases the duplex stability and increase target specificity.

Finally, one would have had an expectation of success given that Agrawal et al. specifically teach duplex stability with modified 2'-O-methyl ribofuranosyl moieties (see Figure 3).

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made

This action is final.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Want can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of

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Kimberly Chong
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